<222> (5)..(5) <223> Xaa is Ser or Thr

SEQUENCE LISTING

```
<110> CALIFORNIA INSTITUTE OF TECHNOLOGY
COPE, Gregory
VERMA, Rati
ARAVIND, L
KOONIN, Eugene
DESHAIES, Raymond
<120> REGULATION OF TARGET PROTEIN ACTIVITY THROUGH MODIFIER PROTEINS
<130> CIT1510-4
<150> US 60/261,314
<151> 2001-01-12
<150> US 60/322.322
<151> 2001-09-14
<150> US 60/322,030
<151> 2001-09-14
<160> 22
<170> PatentIn version 3.1
<210> 1
<211> 14
<212> PRT
<213> Artificial sequence
<220>
<223> JAM domain
<220>
<221> MISC FEATURE
<222> (1)..(14)
<223> Xaa is any amino acid
<400> 1
His Xaa His Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asp
1
                5
<210> 2
<211> 17
<212> PRT
<213> Artificial sequence
<220>
<223> JAM domain
<220>
<221> MISC FEATURE
<222> (3)..(3)
<223> Xaa is Tyr or Ile
<220>
<221> MISC_FEATURE
```

145

150

155

```
<220>
<221> MISC FEATURE
<222>
      (8)..(16)
<223> Xaa is any amino acid
<400> 2
Gly Trp Xaa His Xaa His Pro Xaa Xaa Xaa Xaa Xaa Xaa Ser Xaa Xaa
                                    10
Asp
<210> 3
<211> 246
<212> PRT
<213> Homo sapiens
<400> 3
Thr Met Ile Ile Met Asp Ser Phe Ala Leu Pro Val Glu Gly Thr Glu
Thr Arg Val Asn Ala Gln Ala Ala Ala Tyr Glu Tyr Met Ala Ala Tyr
Ile Glu Asn Ala Lys Gln Val Gly Arg Leu Glu Asn Ala Ile Gly Trp
Tyr His Ser His Pro Gly Tyr Gly Cys Trp Leu Ser Gly Ile Asp Val
Ser Thr Gln Met Leu Asn Gln Gln Phe Gln Glu Pro Phe Val Ala Val
Val Ile Asp Pro Thr Arg Thr Ile Ser Ala Gly Lys Val Asn Leu Gly
Ala Phe Arg Thr Tyr Pro Lys Gly Tyr Lys Pro Pro Asp Glu Gly Pro
                                105
                                                    110
Ser Glu Tyr Gln Thr Ile Pro Leu Asn Lys Ile Glu Asp Phe Gly Val
        115
                            120
                                                125
His Cys Lys Gln Tyr Tyr Ala Leu Glu Val Ser Tyr Phe Lys Ser Ser
Leu Asp Arg Lys Leu Leu Glu Leu Leu Trp Asn Lys Tyr Trp Val Asn
```

Thr Leu Ser Ser Ser Ser Leu Leu Thr Asn Ala Asp Tyr Thr Thr Gly $165 \\ 165 \\ 170 \\ 175$

Gln Val Phe Asp Leu Ser Glu Lys Leu Glu Gln Ser Glu Ala Gln Leu 180 \$180\$

Gly Arg Gly Ser Phe Met Leu Gly Leu Glu Thr His Asp Arg Lys Ser 195 $\,$ 200 $\,$ 205

Glu Asp Lys Leu Ala Lys Ala Thr Arg Asp Ser Cys Lys Thr Thr Ile 210 215 220

Glu Ala Ile His Gly Leu Met Ser Gln Val Ile Lys Asp Lys Leu Phe 225 230 235

Asn Gln Ile Asn Ile Ser 245

<210> 4 <211> 245 <212> PRT

<213> Homo sapiens

<400> 4

Val Ser Val Glu Ala Val Asp Pro Val Phe Gln Ala Lys Met Leu Asp 20 25 30

Met Leu Lys Gln Thr Gly Arg Pro Glu Met Val Val Gly Trp Tyr His $35 \ \ 40 \ \ \ 45$

Ser His Pro Gly Phe Gly Cys Trp Leu Ser Gly Val Asp Ile Asn Thr 50 55 60

Gln Gln Ser Phe Glu Ala Leu Ser Glu Arg Ala Val Ala Val Val 65 70 75 80

Asp Pro Ile Gln Ser Val Lys Gly Lys Val Val Ile Asp Ala Phe Arg 85 90 95

Leu Ile Asn Ala Asn Met Met Val Leu Gly His Glu Pro Arg Gln Thr

Thr Ser Asn Leu Gly His Leu Asn Lys Pro Ser Ile Gln Ala Leu Ile 115 120 125

His Gly Leu Asn Arg His Tyr Tyr Ser Ile Thr Ile Asn Tyr Arg Lys 130 135 140

Asn Glu Leu Glu Gln Lys Met Leu Leu Asn Leu His Lys Lys Ser Trp 145 150 155 160

Met Glu Gly Leu Thr Leu Gln Asp Tyr Ser Glu His Cys Lys His Asn 165 170

Glu Ser Val Val Lys Glu Met Leu Glu Leu Ala Lys Asn Tyr Asn Lys 180 185 190

Ala Val Glu Glu Glu Asp Lys Met Thr Pro Glu Gln Leu Ala Ile Lys 195 200

Asn Val Gly Lys Gln Asp Pro Lys Arg His Leu Glu Glu His Val Asp 210 215

Val Leu Met Thr Ser Asn Ile Val Gln Cys Leu Ala Ala Met Leu Asp 230

Thr Val Val Phe Lys 245

<210> 5 <211> 421 <212> PRT

<213> Homo sapiens

<400> 5

Met Pro Asp His Thr Asp Val Ser Leu Ser Pro Glu Glu Arg Val Arg

Ala Leu Ser Lys Leu Gly Cys Asn Ile Thr Ile Ser Glu Asp Ile Thr

Pro Arg Arg Tyr Phe Arg Ser Gly Val Glu Met Glu Arg Met Ala Ser

Val Tyr Leu Glu Glu Gly Asn Leu Glu Asn Ala Phe Val Leu Tyr Asn 55

Lys Phe Ile Thr Leu Phe Val Glu Lys Leu Pro Asn His Arg Asp Tyr 70 75

Gln Gln Cys Ala Val Pro Glu Lys Gln Asp Ile Met Lys Lys Leu Lys 85 90 95

Glu Ile Ala Phe Pro Arg Thr Asp Glu Leu Lys Asn Asp Leu Leu Lys $100 \\ 105 \\ 110$

Lys Tyr Asn Val Glu Tyr Gln Glu Tyr Leu Gln Ser Lys Asn Lys Tyr 115 120 125

Lys Ala Glu Ile Leu Lys Lys Leu Glu His Gln Arg Leu Ile Glu Ala 130 135 140

Glu Arg Lys Arg Ile Ala Gln Met Arg Gln Gln Gln Leu Glu Ser Glu 145 150 155 160

Gln Phe Leu Phe Phe Glu Asp Gln Leu Lys Lys Gln Glu Leu Ala Arg \$165\$

Gly Gln Met Arg Ser Gln Gln Thr Ser Gly Leu Ser Glu Gln Ile Asp $180 \,$ $\,$ $185 \,$ $\,$ $190 \,$

Gly Ser Ala Leu Ser Cys Phe Ser Thr His Gln Asn Asn Ser Leu Leu 195 200 205

Asn Val Phe Ala Asp Gln Pro Asn Lys Ser Asp Ala Thr Asn Tyr Ala 210 215 220

Ser His Ser Pro Pro Val Asn Arg Ala Leu Thr Pro Ala Ala Thr Leu 225 230 235 240

Ser Ala Val Gln Asn Leu Val Val Glu Gly Leu Arg Cys Val Val Leu 245 250 250

Pro Glu Asp Leu Cys His Lys Phe Leu Gln Leu Ala Glu Ser Asn Thr 260 265 270

Val Arg Gly Ile Glu Thr Cys Gly Ile Leu Cys Gly Lys Leu Thr His 275 280 285

Asn Glu Phe Thr Ile Thr His Val Ile Val Pro Lys Gln Ser Ala Gly 290 295 300

Pro Asp Tyr Cys Asp Met Glu Asn Val Glu Glu Leu Phe Asn Val Gln 305 \$310\$ 315 320

Asp Gln His Asp Leu Leu Thr Leu Gly Trp Ile His Thr His Pro Thr \$325\$ \$330\$

Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His Cys Ser Tyr \$340\$ \$345\$

Gln Leu Met Leu Pro Glu Ala Ile Ala Ile Val Cys Ser Pro Lys His 355 \$360\$

Lys Asp Thr Gly Ile Phe Arg Leu Thr Asn Ala Gly Met Leu Glu Val $_{\rm 370}$ $_{\rm 375}$

Ser Ala Cys Lys Lys Gly Phe His Pro His Thr Lys Glu Pro Arg 385 390 395 400

Leu Phe Ser Ile Cys Lys His Val Leu Val Lys Asp Ile Lys Ile Ile 405 \$415\$

Val Leu Asp Leu Arg 420

<210> 6 <211> 461

<212> PRT <213> Homo sapiens

<400> 6

Met Asp Gln Pro Phe Thr Val Asn Ser Leu Lys Lys Leu Ala Ala Met 1 $$ 5 $$ 10 $$ 15

Pro Asp His Thr Asp Val Ser Leu Ser Pro Glu Glu Arg Val Arg Ala

Leu Ser Lys Leu Gly Cys Asn Ile Thr Ile Ser Glu Asp Ile Thr Pro \$35\$

Arg Arg Tyr Phe Arg Ser Gly Val Glu Met Glu Arg Met Ala Ser Val 50 60

Tyr Leu Glu Glu Gly Asn Leu Glu Asn Ala Phe Val Leu Tyr Asn Lys 65 70 75 80

Phe Ile Thr Leu Phe Val Glu Lys Leu Pro Asn His Arg Asp Tyr Gln 85 90 95

Gln Cys Ala Val Pro Glu Lys Gln Asp Ile Met Lys Lys Leu Lys Glu

100 105 110

Ile Ala Phe Pro Arg Thr Asp Glu Leu Lys Asn Asp Leu Leu Lys Lys 115 120 125

Tyr Asn Val Glu Tyr Gln Glu Tyr Leu Gln Ser Lys Asn Lys Tyr Lys 130 135 140

Ala Glu Ile Leu Lys Lys Leu Glu His Gln Arg Leu Ile Glu Ala Glu 145 \$150\$

Arg Lys Arg Ile Ala Gln Met Arg Gln Gln Gln Leu Glu Ser Glu Gln 165 170 175

Phe Leu Phe Phe Glu Asp Gln Leu Lys Lys Gln Glu Leu Ala Arg Gly 180 185 190

Gln Met Arg Ser Gln Gln Thr Ser Gly Leu Ser Glu Gln Ile Asp Gly 195 \$200\$

Val Phe Ala Asp Gln Pro Asn Lys Ser Asp Ala Thr Asn Tyr Ala Ser 225 230235235

His Ser Pro Pro Val Asn Arg Ala Leu Thr Pro Ala Ala Thr Leu Ser $245 \hspace{1.5cm} 250 \hspace{1.5cm} 255$

Ala Val Gl
n Asn Leu Val Val Glu Gly Leu Arg Cys Val Val Leu Pro
 260 265 270

Glu Asp Leu Cys His Lys Phe Leu Gln Leu Ala Glu Ser Asn Thr Val 275 280 285

Arg Gly Ile Glu Thr Cys Gly Ile Leu Cys Gly Lys Leu Thr His Asn 290 295 300

Glu Phe Thr Ile Thr His Val Ile Val Pro Lys Gln Ser Ala Gly Pro 305 $$ 310 $$ 315 $$ 320

Asp Tyr Cys Asp Met Glu Asn Val Glu Glu Leu Phe Asn Val Gln Asp 325 330 335

Gln His Asp Leu Leu Thr Leu Gly Trp Ile His Thr His Pro Thr Gln \$340\$

Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His Cys Ser Tyr Gln 355 360

Leu Met Leu Pro Glu Ala Ile Ala Ile Val Cvs Ser Pro Lvs His Lvs 370 375 380

Asp Thr Gly Ile Phe Arg Leu Thr Asn Ala Gly Met Leu Glu Val Ser 385 390 395 400

Ala Cvs Lvs Lvs Lvs Glv Phe His Pro His Thr Lvs Glu Pro Arg Leu 405 410 415

Phe Ser Ile Gln Lys Phe Leu Ser Gly Ile Ile Ser Gly Thr Ala Leu 425 420

Glu Met Glu Pro Leu Lys Ile Gly Tyr Gly Pro Asn Gly Phe Pro Leu 435 440 445

Leu Gly Ile Ser Arg Ser Ser Ser Pro Ser Glu Gln Leu 450 455

<210> 7

<211> 424 <212> PRT <213> Homo sapiens

<400> 7

Met Ser Asp His Gly Asp Val Ser Leu Pro Pro Glu Asp Arg Val Arg

Ala Leu Ser Gln Leu Glv Ser Ala Val Glu Val Asn Glu Asp Ile Pro 25

Pro Arg Arg Tyr Phe Arg Ser Gly Val Glu Ile Ile Arg Met Ala Ser

Ile Tyr Ser Glu Glu Gly Asn Ile Glu His Ala Phe Ile Leu Tyr Asn

Lys Tyr Ile Thr Leu Phe Ile Glu Lys Leu Pro Lys His Arg Asp Tyr

Lys Ser Ala Val Ile Pro Glu Lys Lys Asp Thr Val Lys Lys Leu Lys 85 90

Glu Ile Ala Phe Pro Lys Ala Glu Glu Leu Lys Ala Glu Leu Lys 100 \$105\$

Arg Tyr Thr Lys Glu Tyr Thr Glu Tyr Asn Glu Glu Lys Lys Lys Glu 115 120 125

Ala Glu Glu Leu Ala Arg Asn Met Ala Ile Gln Glu Glu Leu Glu Lys 130 $$135\$

Glu Lys Gln Arg Val Ala Gln Gln Lys Gln Gln Gln Leu Glu Gln Glu 145 $$ 150 $$ 155 $$ 160

Gln Phe His Ala Phe Glu Glu Met Ile Arg Asn Gln Glu Leu Glu Lys \$165\$ \$170\$ \$175\$

Glu Arg Leu Lys Ile Val Gln Glu Phe Gly Lys Val Asp Pro Gly Leu 180 \$185\$

Gly Gly Pro Leu Val Pro Asp Leu Glu Lys Pro Ser Leu Asp Val Phe $195 \hspace{0.5in} 200 \hspace{0.5in} 205 \hspace{0.5in}$

Val Arg Pro Ala Lys Pro Pro Val Val Asp Arg Ser Leu Lys Pro Gly 225 230 235

Ala Leu Ser Asn Ser Glu Ser Ile Pro Thr Ile Asp Gly Leu Arg His 245 250 255

Val Val Pro Gly Arg Leu Cys Pro Gln Phe Leu Gln Leu Ala Ser 260 265 270

Ala Asn Thr Ala Arg Gly Val Glu Thr Cys Gly Ile Leu Cys Gly Lys 275 280 285

Leu Met Arg Asn Glu Phe Thr Ile Thr His Val Leu Ile Pro Lys Gln 290 295 300

Ser Ala Gly Ser Asp Tyr Cys Asn Thr Glu Asn Glu Glu Glu Leu Phe 305 \$310\$ 315 320

Leu Ile Gln Asp Gln Gln Gly Leu Ile Thr Leu Gly Trp Ile His Thr 325 330 335

His Pro Thr Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His

Cys Ser Tyr Gln Met Met Leu Pro Glu Ser Val Ala Ile Val Cys Ser $355 \hspace{1.5cm} 360 \hspace{1.5cm} 365 \hspace{1.5cm}$

Glu Glu Ile Ser Ser Cys Arg Gln Lys Gly Phe His Pro His Ser Lys 385 \$390\$ 395 400

Asp Pro Pro Leu Phe Cys Ser Cys Ser His Val Thr Val Val Asp Arg $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415 \hspace{1.5cm}$

Ala Val Thr Ile Thr Asp Leu Arg 420

<210> 8 <211> 58

<212> PRT

<213> Homo sapiens

<400> 8

Val Gly Arg Leu Glu Asn Ala Ile Gly Trp Tyr His Ser His Pro Gly 1 $\,$ 15

Tyr Gly Cys Trp Leu Ser Gly Ile Asp Val Ser Thr Gln Met Leu Asn $20 \\ 25 \\ 30$

Gln Gln Phe Gln Glu Pro Phe Val Ala Val Val Ile Asp Pro Thr Arg

Thr Ile Ser Ala Gly Lys Val Asn Leu Gly

<210> 9

<211> 58 <212> PRT

<213> Drosophila melanogaster

<400> 9

Tyr Gly Cys Trp Leu Ser Gly Ile Asn Val Ser Thr Gln Met Leu Asn 20 25 30

Gln Thr Tvr Gln Glu Pro Phe Val Ala Ile Val Val Asp Pro Val Arg 35 40

Thr Val Ser Ala Gly Lys Val Cys Leu Gly 50

<210> 10

<211> 58 <212> PRT

<213> Arabidopsis thaliana

<400> 10

Ala Gly Arg Leu Glu Asn Val Val Gly Trp Tyr His Ser His Pro Gly 10

Tyr Gly Cys Trp Leu Ser Gly Ile Asp Val Ser Thr Gln Arg Leu Asn 20 25

Gln Gln His Gln Glu Pro Phe Leu Ala Val Val Ile Asp Pro Thr Arg 35 40

Thr Val Ser Ala Gly Lys Val Glu Ile Gly

<210> 11

<211> 58

<212> PRT

<213> Caenorhabditis elegans

<400> 11

Glu Gly Arg Lys Glu Lys Val Val Gly Trp Tyr His Ser His Pro Gly 5

Tyr Gly Cys Trp Leu Ser Gly Ile Asp Val Ser Thr Gln Thr Leu Asn 20 25

Gln Lys Phe Gln Glu Pro Trp Val Ala Ile Val Ile Asp Pro Leu Arg

Thr Met Ser Ala Gly Lys Val Asp Ile Gly

<210> 12

<211> 58 <212> PRT

<213> Archaeoglobus fulgidus

<400> 12

Leu Pro Ile Gly Met Lys Val Phe Gly Thr Val His Ser His Pro Ser 1 $$ 5 $$ 10 $$ 15

Pro Ser Cys Arg Pro Ser Glu Glu Asp Leu Ser Leu Phe Thr Arg Phe 20 25 30

Gly Lys Tyr His Ile Ile Val Cys Tyr Pro Tyr Asp Glu Asn Ser Trp 35 40 45

Lys Cys Tyr Asn Arg Lys Gly Glu Glu Val

<210> 13

<211> 58

<212> PRT <213> Pyrococcus horikoshii

<400> 13

Met Pro His Asp Glu Ser Ile Lys Gly Thr Phe His Ser His Pro Ser 1 5 10 15

Pro Phe Pro Tyr Pro Ser Glu Gly Asp Leu Met Phe Phe Ser Lys Phe $20 \ \ 25 \ \ 30$

Gly Gly Ile His Ile Ile Ala Ala Phe Pro Tyr Asp Glu Asp Ser Val\$35\$ 40 45

Lys Ala Phe Asp Ser Glu Gly Arg Glu Val 50 55

<210> 14

<211> 58 <212> PRT

<213> Thermoplasma volcanium

<400> 14

Lys Pro Ile Asp Phe Ser Leu Val Gly Ser Val His Ser His Pro Ser 1 $$ 5 $$ 10 $$ 15

Gly Ile Thr Lys Pro Ser Asp Glu Asp Leu Arg Met Phe Ser Leu Thr 20 25 30

Gly Lys Ile His Ile Ile Val Gly Tyr Pro Tyr Asn Leu Lys Asp Tyr 35 40 45

Ser Ala Tyr Asp Arg Ser Gly Asn Lys Val 50 55

```
<210> 15
<211> 58
<212> PRT
<213> Methanobacterium thermoautotrophicum
<400> 15
Leu Pro Pro Phe Thr Gly Ala Val Gly Ser Val His Ser His Pro Gly
Pro Val Asn Leu Pro Ser Ala Ala Asp Leu His Phe Phe Ser Lys Asn
           20
                              25
                                                  30
Gly Leu Phe His Leu Ile Ile Ala His Pro Tyr Thr Met Glu Thr Val
       35
                           40
Ala Ala Tyr Thr Arg Asn Gly Asp Pro Val
   50
<210> 16
<211> 58
<212> PRT
<213> Aquifex aeolicus
<400> 16
Ile Ser Lys Gly Met Glu Ile Val Gly Val Tyr His Ser His Pro Asp
                                   10
His Pro Asp Arg Pro Ser Gln Phe Asp Leu Gln Arg Ala Phe Pro Asp
                               25
Leu Ser Tyr Ile Ile Phe Ser Val Gln Lys Gly Lys Val Ala Ser Tyr
                           40
Arg Ser Trp Glu Leu Lys Gly Asp Lys Phe
<210> 17
<211> 60
<213> Mycobacterium tuberculosis
<400> 17
Glu Asp Ala Asp Glu Val Pro Val Val Ile Tyr His Ser His Thr Ala
```

Thr Glu Ala Tyr Pro Ser Arg Thr Asp Val Lys Leu Ala Thr Glu Pro $20 \hspace{1cm} 25 \hspace{1cm} 30 \hspace{1cm}$

Asp Ala His Tyr Val Leu Val Ser Thr Arg Asp Pro His Arg His Glu 35 40 45

Leu Arg Ser Tyr Arg Ile Val Asp Gly Ala Val Thr 50 55 60

<210> 18

<211> 58

<212> PRT

<213> Escherichia coli

<400> 18

Ile Lys Ile Asn Ala Ser Ala Leu Ile Leu Ala His Asn His Pro Ser 1 $$ 5 $$ 10 $$ 15

Gly Cys Ala Glu Pro Ser Lys Ala Asp Lys Leu Ile Thr Glu Arg Ile $20 \ 25 \ 30 \$

Ile Lys Ser Cys Gln Phe Met Asp Leu Arg Val Leu Asp His Ile Val \$35\$

Ile Gly Arg Gly Glu Tyr Val Ser Phe Ala

<210> 19

<211> 57

<212> PRT

<213> Drosophila melanogaster

<400> 19

Thr Gly Arg Pro Glu Met Val Val Gly Trp Tyr His Ser His Pro Gly 1 5 10 15

Phe Gly Cys Trp Leu Ser Gly Val Asp Ile Asn Thr Gln Gln Ser Phe

Glu Ala Leu Ser Glu Arg Ala Val Ala Val Val Val Asp Pro Ile Gln 35 40 45

Ser Val Lys Gly Lys Val Val Ile Asp

<210> 20

<211> 57 <212> PRT

<213> Homo sapiens

<400> 20

Thr Gly Arg Pro Glu Met Val Val Gly Trp Tyr His Ser His Pro Gly 1 $$ 10 $$ 15

Phe Gly Cys Trp Leu Ser Gly Val Asp Ile Asn Thr Gln Gln Ser Phe 20 25 30

Glu Ala Leu Ser Glu Arg Ala Val Ala Val Val Val Asp Pro Ile Gln 35 40 45

Ser Val Lys Gly Lys Val Val Ile Asp

<210> 21

<211> 57 <212> PRT

<213> Dictyostelium discoideum

<400> 21

Thr Gly Arg Asp Glu Ile Val Ile Gly Trp Tyr His Ser His Pro Gly 1 5 10 15

Phe Gly Cys Trp Leu Ser Ser Val Asp Val Asn Thr Gln Gln Ser Phe 20 25 30

Glu Gln Leu Gln Ser Arg Ala Val Val Val Val Val Asp Pro Leu Gln 35 40 45

Ser Val Arg Gly Lys Val Val Ile Asp

<210> 22 <211> 57

<211> 57 <212> PRT

<213> Saccharomyces cerevisiae

<400> 22

Thr Gly Arg Asp Gln Met Val Val Gly Trp Tyr His Ser His Pro Gly $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Phe Gly Cys Trp Leu Ser Ser Val Asp Val Asn Thr Gln Lys Ser Phe 20 25 30

Glu Gln Leu Asn Ser Arg Ala Val Ala Val Val Val Asp Pro Ile Gln 35 40 45

Ser Val Lys Gly Lys Val Val Ile Asp 50 55